AMERICAN JOURNAL OF EPIDEMIOLOGY
Vol. 121, No. 1
Copyright © 1985 by The Johns Hopkins University School of Hygiene and Public Health
All rights reserved
Printed in U.S.A.

PASSIVE SMOKING IN ADULTHOOD AND CANCER RISK[1]

DALE P. SANDLER, RICHARD B. EVERSON AND ALLEN J. WILCOX

Sandler, D. P. (National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709), R. B. Everson and A. J. Wilcox. Passive smoking in adulthood and cancer risk. *Am J Epidemiol* 1985;121:37-48.

Overall cancer risk from adult passive smoking has been examined using smoking by spouse as the measure of exposure. Information on smoking by spouse was obtained for 518 cancer cases and 518 noncancer controls. Cancer cases were identified from a hospital-based tumor registry in North Carolina. Cases included all sites except basal cell cancer of the skin and were between the ages of 15 and 59 years at the time of diagnosis. Cancer risk among individuals ever married to smokers was 1.6 times that among those never married to smokers ($p = 0.01$). This increased risk was not explained by confounding by individual smoking habits, demographic characteristics, or social class. Elevated risks were [redacted] cancer sites and were not limited to lung cancer or other "smoking-related" tumors. Risks from passive smoking appeared greater among groups generally at lower cancer risk (females, nonsmokers, and individuals younger than age 50 years), but were not limited to these groups.

neoplasms; risk; smoking; tobacco smoke pollution

Passive exposure to cigarette smoke has been linked with a variety of health consequences in humans, including bronchitis and pneumonia in infants (1), reduced pulmonary function (2) and acute respiratory disease in children (3–5), and decreased airway function in otherwise healthy adults (6). Several reports have also focused attention on a possible association between passive exposure to cigarette smoke and lung cancer (7–10).

In a case-control study by Trichopoulos and colleagues (7), 51 white females with lung cancer and 163 controls from an orthopedic service were compared with regard to smoking histories of husbands. Women who were not smokers but were married to smokers were at two- to threefold risk for lung cancer compared with nonsmoking women who were not married to smokers. An updated report of this study involving 77 nonsmoking lung cancer cases and 225 nonsmoking controls confirmed the twofold risk among passive smokers (8). In a prospective study from Japan, Hirayama (9) observed 245 lung cancer deaths among 91,000 married women. The lung cancer death rate for nonsmoking women married to smokers was nearly twice that for nonsmoking women married to nonsmokers and was one-half that for women who themselves smoked. Emphysema was the only other cause of death to exhibit such a pattern, although the trend was not statis-

Received for publication January 23, 1984, and in final form April 12, 1984.

[1] From the Epidemiology Branch, Biometry and Risk Assessment Program, National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Reprint requests to Dr. Dale P. Sandler, Epidemiology Branch, Mail Drop A3-02, National Institute of Environmental Health Sciences, P. O. Box 12233, Research Triangle Park, NC 27709.

The authors thank Dr. James P. Browder and the staff of the Cancer Data Base, North Carolina Memorial Hospital for allowing the use of the tumor registry for case identification, and David L. Shore, Karen L. Milne, and Sue W. Ward for assisting in data management and analysis.

2023513158

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

tically significant. Most recently, Correa et al. (10) reported a twofold risk for lung cancer among nonsmokers married to smokers. In contrast, analysis of data from an American Cancer Society study in the United States failed to demonstrate an association between passive exposure to cigarette smoke and lung cancer risk (11).

Many of the constituents of mainstream cigarette smoke which is actively inhaled by the smoker are present in reduced quantity in exhaled smoke (12) which is then passively inhaled by the nonsmoker. These same constituents are also contained in sidestream smoke which is released from the cigarette between active puffs and is also inhaled by the passive smoker. One might expect to find, as did Hirayama (9) for lung cancer, that for smoking-related sites, the cancer risk in individuals passively exposed to cigarette smoke might fall between that for smokers and that for nonsmokers. Risk from passive smoking might also be expected to be much lower than that from direct smoking.

However, some chemicals appear in higher concentration in sidestream smoke than in mainstream smoke, making the exposure from passive smoking qualitatively different (12, 13). The health consequences from passive smoking may, therefore, differ from those of direct smoking. These chemicals, many of which are known carcinogens, might lead to increased risk for cancer at sites not shown to be related to direct exposure to cigarette smoke. In comparing sidestream with mainstream smoke, Brunnemann (in refs. 12 and 13) found 52 times as much dimethylnitrosamine, 16 times as much naphthalene, 28 times as much methylnaphthalene, 3.4 times as much benzo(α)pyrene, and 5.6 times as much toluene, for example, in sidestream smoke as in mainstream smoke. While the concentrations of these chemicals are higher than in mainstream smoke, actual exposure from passive smoking is heavily influenced by the amount of smoke generated, the volume of ambient air, room ventilation, and the manner in which the cigarettes are smoked.

Differences in the route of inhalation of sidestream and mainstream smoke might also account for differences in site-specific effects. Wynder and Goodman (14), for example, have proposed that if sidestream smoke components are inhaled through the nasal passages, gaseous components but not smoke particulates would reach the lung.

As a preliminary exploration of the hypothesis that passive exposure to cigarette smoke may be carcinogenic, we examined adult passive exposure to cigarette smoke in relationship to cancers of all sites. Since active and passive smokers may differ in the mix of carcinogens to which they are exposed, it is not obvious which sites might be at highest risk of cancer among passive smokers. Since active smokers are also passively exposed, candidate sites might be drawn from those that have been linked with active smoking. However, there may be additional sites whose relationship to smoking has been obscured. In studies comparing smokers with nonsmokers, passive smokers are often included in the nonsmoking group. This would make it difficult to detect small differences in risk due to passive smoking. We report here on cancer risk from passive smoking using smoking histories of spouses as a measure of passive exposure to cigarette smoke during adulthood.

METHODS

Data reported here are from a study of childhood exposure to cigarette smoke and cancer risk in adulthood (29). Cases for study were selected from the hospital-based tumor registry at the North Carolina Memorial Hospital of the University of North Carolina in Chapel Hill. They included all cases diagnosed between July 1, 1979 and March 31, 1981 and assumed to be alive as of March 31, 1981. Cases were between the ages of 15 and 59 years at the time of diagnosis and included all cancer sites ex-

2023513159

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

cept basal cell cancer of the skin. Cases were restricted to this age group to maximize the likelihood of also detecting effects from childhood exposure to cigarette smoke. Individuals older than 60 years in 1981 are not likely to have had mothers who smoked. Patients with multiple primary tumors were included only if the first primary tumor was diagnosed during the study period.

Cases were mailed a questionnaire for self-completion. This mailing was followed by a second mailing and then a telephone call if needed. In addition to questions on exposure to cigarette smoke, cases were asked to identify friends or acquaintances who did not have cancer to serve as comparison subjects. These friends were the same race, sex, and age (±5 years) as the cases. Approximately 60 per cent of the controls were identified in this manner. For cases for whom friend controls were not successfully obtained, population controls were identified by systematic telephone sampling. Beginning with the telephone numbers of the cases, the next higher or lower telephone numbers were called until individuals of the same race, sex, and age (±5 years) were found. For cases interviewed by telephone, the calls to identify controls were made at the same time of day. For cases contacted by mail, telephone controls were chosen during randomly assigned times of day.

Of 740 eligible cancer cases identified from the tumor registry, 107 (14 per cent) died before we could contact them. An additional 115 (15 per cent) either refused (n = 71) to participate or could not be contacted. In all, completed questionnaires were obtained for 518 (70 per cent) of the eligible cases.

Of 518 cases, 360 (70 per cent) named friends or acquaintances who could be contacted as controls. Of these, 86 per cent were successfully contacted for an overall response rate of 60 per cent. To obtain the additional 209 controls, 1,237 households were telephoned. Screening data (age, race, sex, and cancer history of household members) were obtained for 988 households (80 per cent); 224 (23 per cent) of these households had a qualifying member. Fifteen (7 per cent) qualifying telephone controls refused to participate. The overall response rate for selection of telephone controls was 75 per cent (80 per cent × 93 per cent). Although not shown here, data were analyzed separately by control selection group, and the adjusted results were identical to those obtained when the control groups were combined.

Procedurally, the control selection process involved one-to-one matching. This was done to allow the selection of population controls without having an enumerated sampling frame. The analyses presented here are for unmatched data to maximize the study sample size following losses due to missing data on exposure. In most comparisons, the factors used in control selection are taken into account by adjustment procedures. Parallel analyses for matched pairs were carried out. Although not presented here, the results were similar.

Passive exposure to cigarette smoke during adulthood was estimated from a questionnaire report of the number of years of marriage during which a spouse smoked. Subjects were considered exposed if they had a spouse who smoked regularly at any time during their marriage. Regular smoking was defined as smoking at least one cigarette per day for as long as six months. The nonexposed group consisted of persons married to nonsmokers and persons who never married. The quantity smoked was reported as the average number of cigarettes smoked per day by a spouse while married to a study subject.

For the analysis of questionnaire data, odds ratios were calculated, and the chi-square test was used to assess statistical significance. Combined estimates of the odds ratio (OR) in stratified analyses were obtained using the Mantel-Haenszel technique (15). The method of Gart (16) was used to obtain 95 per cent confidence limits

2023513160

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

for the combined estimates of the odds ratio. When the 95 per cent confidence limits did not include unity, the odds ratio was considered statistically significant ($p < 0.05$). Level of education was reported as number of years of school completed and occupation was given as usual occupation. For stratified and adjusted analyses, age and level of education were treated as categorical variables with four levels of age (<30, 30–39, 40–49, and 50+ years) and three levels of education (<12 years, 12 years, and >12 years).

Results

The distribution of cases by cancer site is shown in table 1. The young age of cases, the referral nature of the hospital, and the fact that the study was limited to living cases account for the distribution of cancers seen. There was a predominance of breast cancers, female genital tract cancers, and leukemia and lymphoma, and a relative lack of respiratory tumors. Eligible cases with respiratory cancer were significantly more likely to die before they could be contacted for this study.

Cases and controls are compared in table 2. Cases and controls are, by design, distributed similarly by race and sex, with 70 per cent of each group white and 67 per cent female. The mean age of cases (43.6 years) and controls (43.5 years) is also similar. Level of education differs significantly between groups; 45 per cent of cases and 36 per cent of controls never graduated from high school. Level of education, therefore, is taken into consideration in most analyses. On the other hand, cases and controls do not differ by broad occupational category. A greater proportion of controls never married (16 per cent vs. 13 per cent), but this difference is not statistically significant. Cancer cases and controls also do not differ in reported smoking histories. In part this is due to the relative absence of lung cancer cases and to the method of control selection. Sixty per cent of controls are friends of cases, and the smoking habits of individuals who are friends may be similar. When only cases with population controls are included, 57 per cent of cases and 46 per cent of population controls were smokers.

The overall crude cancer risk for individuals ever married to smokers is 1.6 times that for those not married to smokers ($p < 0.01$) (table 3). Adjusting independently

TABLE 1

Distribution of cancer cases by site of primary tumor and study status

Site	ICD* No.	Included		Refused or lost	
		No.	(%)	No.	(%)
Lip, oral cavity, and pharynx	140–149	22	(4)	15	(7)
Digestive organs and peritoneum	150–159	41	(8)	16	(7)
Respiratory and intrathoracic organs	160–165	32	(6)	43	(19)†
Bone, connective tissue, and skin	170–173	42	(8)	13	(6)
Breast	174	60	(12)	16	(7)
Female genital organs	179–184	175	(34)	61	(28)
Prostate	185	10	(2)	0	(0)
Testis	186	6	(1)	3	(1)
Urinary tract	188, 189	6	(1)	9	(4)
Eye, brain, and other nervous system	190–192	38	(7)	20	(9)
Thyroid and other endocrine glands	193, 194	27	(5)	3	(1)
Lymphatic and hematopoietic tissue	200–207	52	(10)	13	(6)
Site unspecified	199	7	(1)	10	(5)
All sites		518	(100.0)	222	(100.0)

* $p < 0.01$.

† ICD, *International Classification of Diseases*, Ninth Revision.

2023513161

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

TABLE 2

Comparison of cases and controls

Factor	Cases No. (%)	Controls No. (%)
Total	518 (100)	518 (100)
Age		
<30	96 (19)	99 (19)
30–39	89 (17)	105 (20)
40–49	132 (25)	121 (23)
50+	201 (39)	193 (37)
Race		
Nonwhite	153 (30)	153 (30)
White	365 (70)	365 (70)
Sex		
Male	169 (33)	169 (33)
Female	349 (67)	349 (67)
Marital status*		
Never married	65 (13)	79 (16)
Ever married	444 (87)	410 (84)
Education†		
<12 years	233 (45)	186 (36)
12 years	137 (27)	186 (36)
>12 years	147 (28)	146 (28)
Occupation‡		
Blue collar	172 (35)	194 (38)
White collar	192 (39)	175 (34)
Housewife	118 (24)	131 (26)
Unemployed	8 (2)	11 (2)
Smoking		
Never	235 (45)	247 (48)
Ever	283 (55)	271 (52)
Current	154 (30)	166 (32)
Past	129 (25)	105 (20)

* Nine cases and 29 controls did not report marital status.

† One case did not report years of education.

‡ Twenty-eight cases and seven controls did not report occupation.

and in combination for sex, age, race, smoking, parental smoking, education, and occupation does not change this finding. Cancer risk from passive exposure to cigarette smoke appears greatest for females and for individuals who are not themselves smokers, with statistically significant risks limited to these subgroups. There are no apparent subgroup differences in risk with race or occupational category (blue collar or white collar), although risk appears greater for individuals with at least a high school education. Cancer risk in relationship to passive exposure to cigarette smoke also appears limited to individuals who are younger than age 50 years.

Cancer risks from passive smoking among smokers and nonsmokers are shown separately in table 4. Risk is clearly elevated among nonsmokers, with the twofold risk significant after adjustment for age, race, or sex. Risk is also elevated among smokers, but the 30 per cent increase in risk is only of borderline statistical significance. Among nonsmokers, risk does not differ with race, but the risk from passive exposure is statistically significant only among females and among individuals between the ages of 30 and 49 years, although it is also elevated for males. For smokers, risk is significantly elevated among females and whites. The twofold risk related to passive exposure among individuals younger than 30 years (table 3) is due to risk among individuals who are themselves smokers (OR = 2.3) (table 4). The lower risk among nonsmokers in this age group (OR = 1.4) contrasts with the greater risk among nonsmokers in the other age categories under age 50 years. This suggests that the cumulative exposure through passive means, alone, for this young group may be below that which would pose a risk.

For most cancer sites, the number of cases is too small for meaningful site-specific analysis. However, statistically significant risks in relationship to passive smoking are seen for breast cancer, cervical cancer, and endocrine cancers. Odds ratios adjusted for possible differences in the distributions of age and level of education are shown in table 5 for smokers and nonsmokers combined.

The twofold risk of breast cancer shown in table 5 is not substantially changed by adjustment for education, race, age, smoking status, or parental smoking. Breast cancer risk is greater among younger women (OR = 3.4 for women <50 years vs. OR = 1.1 for women ≥50 years) and those with at least a high school education (OR = 3.3 vs. OR = 1.0).

The twofold risk for cervical cancer

2023513162

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

TABLE 5

Overall cancer risk from smoking by spouse, adjusted separately† for potential confounding factors

Factor	% exposed‡		Crude OR†	Adjusted OR	95% CL† on adjusted OR
	Cases§ (n = 508)	Controls (n = 489)			
Crude risk	55	43	1.6**		(1.3, 2.1)
Sex					
Male	35	26	1.5**		
Female	65	51	1.8**	1.7**	(1.3, 2.2)
Age					
<30	39	24	2.0*		
30-39	55	39	1.9*	1.6**	(1.3, 2.1)
40-49	67	47	2.2**		
50+	56	54	1.2		
Race					
Nonwhite	50	34	1.6*		
White	58	45	1.7**	1.6**	(1.3, 2.1)
Smoking					
Nonsmokers	52	34	2.1**		
Smokers	58	51	1.3	1.6**	(1.3, 2.1)
Education					
<12 years	55	52	1.1		
12 years	61	35	2.9**	1.6**	(1.2, 2.1)
>12 years	50	41	1.5		
Occupation¶					
Blue collar	53	40	1.7*		
White collar	53	40	1.7*	1.7**	(1.2, 2.3)
Either parent smoked					
No	55	41	1.8**	1.8**	(1.3, 2.3)
Yes	57	44	1.7**		

* $p < 0.05$.

** $p < 0.01$.

† OR, odds ratio, after multiple adjustment for age, race, sex, education, and smoking status = 1.7, 95% confidence limits (CL) = (1.3, 2.3).

‡ Spouse ever smoked while married to study subject.

§ Numbers of cases are not equivalent to those shown in table 1 because of missing values for education or spouse smoking.

¶ Excludes housewives, those unemployed, and those missing data on occupation.

among individuals passively exposed to cigarette smoke is also not affected by adjustment for age, race, smoking status, or smoking by parents. The estimated risk is reduced somewhat by adjustment for level of education, but there is no clear pattern of risk with level of education. As for the other sites, risk appears greatest among younger women (OR = 2.9 for women <50 years vs. OR = 0.9 for women ≥50 years). Odds ratios are statistically significant for whites and for nonsmokers, but the magnitude of the risks for nonwhites and for smokers is similar.

There is also a statistically significant risk of endocrine tumors among exposed individuals, which remains after adjustment for potential confounding variables. In subgroup analyses, risk is significant for younger individuals, nonsmokers, individuals with a high school education, and individuals whose parents did not smoke.

Although the number of lung cancer cases is small ($n = 22$), lung cancer risk from passive exposure to cigarette smoking is examined in table 6 because of current interest in this site. The overall crude risk of 1.9 is not statistically significant. However, the odds ratios for females (OR = ∞) and for nonsmokers (OR = ∞) are statisti-

2023513163

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

TABLE 4

Overall cancer risk from passive exposure to cigarette smoke among smokers and nonsmokers, adjusted for potential confounding factors

Factor	Nonsmokers (n = 466)				Smokers (n = 532)			
	Cases†	Controls	Crude OR‡	Adjusted OR‡ (95% CL§)	Cases†	Controls	Crude OR‡	Adjusted OR‡ (95% CL§)
	No. (% exposed)	No. (% exposed)			No. (% exposed)	No. (% exposed)		
Crude risk	231 (52)	235 (34)	2.1**		278 (58)	254 (51)	1.3	
				(1.4, 3.0)				(0.9, 1.9)
Age								
<30	45 (22)	58 (17)	1.4		50 (54)	38 (34)	2.3	
30–39	36 (56)	49 (31)	2.8*	2.0**	51 (55)	48 (48)	1.3	1.4
40–49	63 (68)	48 (33)	4.3**	(1.4, 2.9)	67 (64)	66 (58)	1.3	(1.0, 1.9)
50+	87 (53)	80 (49)	1.2		110 (58)	102 (55)	1.1	
Sex								
Male	39 (13)	57 (9)	1.5	2.0**	128 (41)	102 (36)	1.2	1.5*
Female	192 (59)	178 (42)	2.0**	(1.3, 2.9)	150 (73)	152 (61)	1.7*	(1.0, 2.1)
Race								
Nonwhite	72 (53)	83 (31)	2.5**	2.0**	77 (47)	63 (48)	1.0	1.4
White	159 (51)	152 (36)	1.9**	(1.4, 3.0)	201 (63)	191 (52)	1.5*	(1.0, 1.9)

* $p < 0.05$.

** $p < 0.01$.

† Numbers of cases are not equivalent to those shown in table 1 because of missing values for spouse smoking.

‡ OR, odds ratio.

§ CL, confidence limits.

cally significant even though they are based on small numbers. Since only two lung cancer cases were nonsmokers and only seven were females, it is not possible to examine lung cancer in greater detail. Risk is also elevated among younger individuals and among those with at least a high school education.

Among nonsmokers alone, risks were significantly elevated for endocrine and cervical cancer, despite the loss of power from reducing the already small number of cases for site-specific analysis (table 7). The twofold risk for breast cancer seen overall is also seen for nonsmokers but is not quite statistically significant. Among smokers, the odds ratio is statistically significant for breast cancer only. However, the approximately twofold risk for cervical cancer is similar to that among nonsmokers.

There is no clear dose-response relationship for all cancer sites combined or for specific sites in relationship to either the number of years married to a smoker (adjusted for age) or the average number of cigarettes smoked per day. This is true for smokers and for nonsmokers and also when analysis is confined to those younger than age 50 years, to whom an effect of passive smoking appears limited.

DISCUSSION

We have found a significantly elevated overall cancer risk for individuals passively exposed to cigarette smoke. This cannot be readily explained by a number of other factors, including individual smoking habits and two measures of social class: education and broad occupational category. Elevated risks were seen for several specific cancer sites and were not limited to lung cancer or other "smoking-related" tumors. These findings might relate to other factors we have not measured or to deficiencies in study design. However, we have not been able to identify a possible confounder or a bias of selection or recall that could have caused the difference in smoking patterns of spouses between cases and controls. Study subjects and interviewers were told

2023513164

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

TABLE 5

Cancer risk from passive exposure to cigarette smoke, adjusted for age and education, all sites combined and specific sites

Site	Cases	Crude OR§	Adjusted OR§	95% CL‖ on adjusted OR§
	No.† (% exposed)‡			
All sites	508 (55)	1.6**	1.6**	(1.2, 2.1)
Lip, oral cavity, and pharynx	22 (55)	1.6	1.1	(0.4, 3.0)
Digestive system	39 (51)	1.4	1.0	(0.5, 2.2)
Respiratory system	32 (50)	1.3	1.0	(0.5, 2.4)
Lung	22 (59)	1.9	1.5	(0.6, 4.3)
Bone, connective tissue, and skin	42 (36)	0.7	0.7	(0.3, 1.5)
Breast¶	59 (69)	2.2**	1.8*	(1.0, 3.7)
Female genital system¶	170 (66)	1.9**	1.8**	(1.2, 2.8)
Cervix	101 (67)	2.0**	1.8*	(1.1, 3.2)
Prostate¶	10 (30)	1.2	0.8	(0.1, 3.9)
Testis¶	5 (40)	1.9	2.6	(0.2, 49.9)
Urinary tract	6 (50)	1.3	1.1	(0.2, 7.6)
Eye, brain, and other nervous system	38 (32)	0.6	0.7	(0.3, 1.5)
Endocrine	26 (65)	2.5*	3.2**	(1.4, 9.4)
Hematopoietic	52 (44)	1.1	1.3	(0.7, 2.5)
Other	7 (57)	1.8	1.8	(0.3, 10.4)

* $p < 0.05$.

** $p < 0.01$.

† Numbers of cases are not equivalent to those shown in table 1 because of missing values for education or spouse smoking.

‡ For comparison, 210 of 489 controls (43%) were exposed.

§ OR, odds ratio.

‖ CL, confidence limits.

¶ Sex-specific comparison. Of 330 female controls, 51% were exposed. Of 159 male controls, 26% were exposed.

simply that the study was designed to look at smoking patterns in families.

Cases and controls were similar with regard to their own smoking histories. This was partly because of the choice of friend controls who tended to have similar smoking histories and because known smoking-related sites were underrepresented in the case population. Cases included in the study were generally younger than those with smoking-related tumors. Unavoidable delays between case identification and completion of interviews also contributed to the lack of smoking-related cancers. Persons with lung cancer and other smoking-related tumors were more likely to have died before they could be interviewed. In addition, because of the special interests of physicians at the hospital from which cases were identified, breast cancers and gynecologic cancers were overrepresented. As a result of this unintentional matching on smoking status, risks from passive smoking and direct smoking cannot be compared.

The route of exposure for the passive smoker is via inhalation. Reports of effects on upper respiratory tract function (2–6) are consistent with this. There has also been a report of mutagens measured in the urine of passive smokers (17), indicating that components of cigarette smoke enter the bloodstream and are circulated throughout the body of the passive smoker. Another report indicated that enzyme activity can be induced by passive exposure to cigarette smoke (18). These findings are tentative, but do suggest that an overall increase in cancer risk or an increase in risk for specific nonrespiratory sites following passive exposure to cigarette smoke is plausible.

2023513165

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

TABLE 6

Lung cancer risk from passive exposure to cigarette smoke, adjusted for potential confounding factors

Factor	Cases (No. (% exposed))	Crude OR†	Adjusted OR†	95% CL‡ on adjusted OR†
Crude risk	22 (59)	1.9		(0.8, 5.0)
Sex				
Male	15 (40)	1.9		(1.1, 8.4)
Female	7 (100)	∞**	3.4*	
Smoking				
Nonsmokers	2 (100)	∞*		
Smokers	20 (55)	1.2	1.5	(0.6, 3.9)
Age				
<50	5 (80)	6.7		
50+	17 (53)	1.0	1.5	(0.6, 3.8)
Education				
<12 years	15 (47)	0.8		
12 years	4 (100)	∞**	1.6	(0.6, 4.4)
>12 years	3 (67)	2.8		
Either parent smoked§				
No	6 (50)	1.5	1.5	(0.5, 4.8)
Yes	9 (56)	1.6		

* $p < 0.05$.
** $p < 0.01$.
† OR, odds ratio.
‡ CL, confidence limits.
§ Numbers reduced because of missing data on parental smoking.

TABLE 7

Cancer risk from passive exposure to cigarette smoke among smokers and nonsmokers: selected sites

Site	Nonsmokers			Smokers		
	No. of cases	Odds ratio	(95% CL†)	No. of cases	Odds ratio	(95% CL†)
Lung	2	∞‡		20	1.2	(0.5, 2.9)
Breast	32	2.0	(0.9, 4.3)	27	2.8*	(1.0, 7.6)
Cervix	56	2.1*	(1.2, 3.9)	45	2.0	(0.9, 4.1)
Endocrine glands	13	4.4*	(1.2, 17.4)	13	1.5	(0.4, 5.5)

* $p < 0.05$.
† CL, confidence limits.
‡ $p = 0.051$.

Our study was intended to consider a range of effects similar to what might be measured in a prospective study of a cohort of individuals who are passively exposed. Such an approach serves to single out sites which appear to be important as well as to investigate whether passive exposure might increase susceptibility to additional insults, thereby increasing cancer risk overall. Two reports in the literature use prospectively collected data (9, 11). One of these (11), however, does not provide data on cancer risks at sites other than the lung, and neither report provides data on overall cancer risk from passive exposure to cigarette smoke. Data from the Japanese study recently presented by Hirayama, however, indicate that cancer risk may be increased at sites other than the lung and that risk may not be limited to smoking-related sites (Hirayama, personal communication: presented at Hawaii Cancer Conference, 1984).

For this study, passive exposure during adult life is determined from a question-

2023513166

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

naire report of the number of years of married life during which a spouse smoked. Misclassification of exposure status is likely for individuals who never married but have lived with other persons who smoked. Slightly more controls than cases reported never marrying, which might lead to differential misclassification. However, we reanalyzed our data, excluding subjects who never married, and found the results to be the same. When only married subjects were included, the odds ratio for cancers of all sites combined was also 1.6. We made no allowances for multiple spouses, other members of the household who smoke, or passive exposures which occur outside of the home. Quantity smoked, too, is an approximate measure. The reported number of cigarettes smoked per day by the spouse is simply the average daily amount smoked during that time period. No allowance was made for changes in smoking habits of the spouse over time or for time since last exposure if the spouse did not smoke during the entire married interval.

Nonetheless, we found smoking by spouse to be significantly associated with overall cancer risk. The odds ratio of 1.6 was not substantially altered by adjustment for age, race, sex, smoking status, education, or occupation. Risk was limited to individuals younger than age 50 years, who were at approximately twofold risk. Risk was also greatest for females and nonsmokers, although not entirely limited to these groups.

When smokers and nonsmokers are considered separately, the twofold risk among nonsmokers is highly-significant and is not altered by adjustment for potential confounding factors. The 30 per cent increase in risk among smokers whose spouses also smoke is only of borderline statistical significance, but is also unchanged by adjustment for other factors. The groups for whom risk from passive smoking appeared greatest are those groups generally at lower cancer risk overall. It may be that the small risk imposed by passive exposure during adult life is difficult to detect statistically in individuals at risk from other causes. Also, women who smoke may tend to smoke less, start later, and inhale differently than men. This would allow for a greater impact of passive exposure among women, regardless of their own smoking status. In addition, very few nonsmoking men are married to smokers, making it more difficult to detect a risk among males. In our data, only 10 per cent (10/96) of nonsmoking males were married to smokers, whereas 51 per cent (189/370) of nonsmoking females were married to smokers.

The increased cancer risk from passive exposure was not limited to sites generally thought to be smoking-related (12, 13). In fact, because of our case selection procedures and delays in interviewing cancer cases, individuals with cancers of smoking-related sites were only a small proportion of total cases. If cancers of the esophagus, respiratory tract, oral cavity and pharynx, urinary tract, and pancreas are designated smoking-related, the odds ratio for smoking-related tumors is 1.3, whereas the odds ratio for other sites is 1.7 ($p < 0.01$). Evidence is accumulating that cancer of the cervix should also be included among those sites that are smoking-related (19–21). When the cervix is included, the odds ratio for smoking-related sites is 2.0 and for other sites is 1.5, both of which are statistically significant.

Only 22 lung cancer cases are included in this report, with an odds ratio of 1.9 among passive smokers. Although not statistically significant, it is consistent with the level of risk reported in other studies. For women and for nonsmokers, the risk of lung cancer among those passively exposed was significantly increased despite very small numbers. The odds ratio for individuals under age 50 years was of borderline significance. Hirayama (9) reported a twofold risk for women married to smokers and found that risks were also greatest among younger women (as measured by husband's age). While Garfinkel (11) didn't find ar

2023513167

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

overall relationship of passive exposure to lung cancer risk, the relative risk among women married to smokers was in the same direction. Relatively few women in Garfinkel's cohort were under age 50 years, which might explain these inconsistent results.

In a study reported by Correa et al. (10), a twofold relative risk was seen among nonsmokers married to smokers. The risks were similar for males and females, although the number of nonsmoking males with lung cancer was very small. Among smokers, males who were light smokers with wives who were heavy smokers had a relative risk of 1.5. Trichopoulos et al. (7, 8) also reported an overall twofold lung cancer risk which was statistically significant among nonsmoking women married to smokers.

The studies reported by Trichopoulos et al. (7, 8), Correa et al. (10), and Hirayama (9) all suggest a dose-response relationship, although different measures of dose were employed in the three studies. In our study, there was no apparent dose-response using either years married to a smoker or average amount smoked by spouse as the measure of dose, but the number of lung cancer cases may be too small to expect a consistent trend. Evaluation of dose is not straightforward and depends on factors which we did not measure, such as room ventilation and smoking "style" of the spouse.

We found a twofold cervical cancer risk, which persisted after adjustment for level of education, among women whose husbands smoked. We did not collect data on sexual activity of cases or spouses. We also see an increased risk of breast cancer. Since the sociodemographic risk factors for these two sites are not the same, this supports the conclusion that the apparent excess cervical cancer risk is not entirely due to confounding by social class. Buckley et al. (22) reported a fourfold risk of cervical cancer among women whose husbands smoked, but after adjustment for number of sexual partners of the husband, the resulting twofold relative risk was not significant. Similar results were reported by Brown et al. (23). Hirayama (9) did not find elevated cervical cancer risk among women whose husbands smoked. This may relate to differences in the ages of the women studied or to differences in risk from other factors.

No previous study has reported a positive association between breast cancer and either passive or direct exposure to cigarette smoke (24–26). In a recently reported study by Rosenberg et al. (27), the relative risk for breast cancer was approximately 1.0 for exsmokers, current smokers, and heavy smokers as compared with nonsmokers. The crude odds ratio of 2.2 that we report is not reduced by adjustment for a number of potential confounding variables. Risk is not seen among women older than age 50 years or among women with less than a high school education, but is fairly constant across all other groups. Petrakis (28) has detected nicotine in breast fluid of nonlactating women who smoked, which may lead to alterations in breast tissue. This would support a possible role for passive smoking if passive exposure also caused such an effect.

One other site for which we find an association with passive exposure, endocrine glands, is not generally thought to be smoking-related. The number of tumors here is small, of which 11 are thyroid tumors.

In summary, passive exposure to smoking by spouse is related to an overall risk of cancer in our data. This association persists after adjusting for possible confounding factors. Associations with several specific tumor sites are also statistically significant, including some which are not ordinarily regarded as smoking-related. Further studies are required to confirm this broad spectrum of carcinogenicity by passive smoking and to explore the unexpected site-specific findings.

References

1. Harlap S, Davies AM. Infant admissions to hospital and maternal smoking. Lancet 1974;1:529-32.
2. Tager IB, Weiss ST, Munoz A, et al. Longitudinal

2023513168

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000

study of the effects of maternal smoking on pulmonary function in children. N Engl J Med 1983;309:699-703.
3. Cameron P, Kostin JS, Zaks JM, et al. The health of smokers' and nonsmokers' children. J Allergy 1969;43:336-41.
4. Norman-Taylor N, Dickinson VA. Dangers for children in smoking families. Community Med 1977;128:32-3.
5. Cameron P, Robertson D. Effect of home environment tobacco smoke on family health. J Appl Psychol 1973;57:142-7.
6. White JR, Froeb HF. Small airways dysfunction in non-smokers chronically exposed to tobacco smoke. N Engl J Med 1980;302:720-3.
7. Trichopoulos D, Kalandidi A, Sparros L, et al. Lung cancer and passive smoking. Int J Cancer 1981;27:1-4.
8. Trichopoulos D, Kalandidi A, Sparros L. Lung cancer and passive smoking: conclusion of Greek study. Lancet 1983;2:677-8.
9. Hirayama T. Non-smoking wives of heavy smokers have a higher risk of lung cancer: a study from Japan. Br Med J 1981;282:183-5.
10. Correa P, Pickle LW, Fontham E, et al. Passive smoking and lung cancer. Lancet 1983;2:595-7.
11. Garfinkel L. Time trends in lung cancer mortality among nonsmokers and a note on passive smoking. JNCI 1981;66:1061-6.
12. United States Department of Health and Human Services. Smoking and health: a report of the Surgeon General. DHHS publication no. (PHS) 79-50066.
13. United States Department of Health and Human Services. The health consequences of smoking—cancer: a report of the Surgeon General. DHHS publication no. (PHS) 82-50179.
14. Wynder EL, Goodman MT. Smoking and lung cancer: some unresolved issues. Epidemiol Rev 1983;5:177-207.
15. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies. JNCI 1959;22:719-48.
16. Gart JJ. Point and interval estimation of the common odds ratio in the combination of 2×2 tables with fixed marginals. Biometrika 1970;57:471-5.
17. Bos RP, Theuws JLG, Henderson PT. Excretion of mutagen in human urine after passive smoking. Cancer Lett 1983;19:85-90.
18. Manchester DK, Jacoby EH. Sensitivity of human placental monooxygenase activity to maternal smoking. Clin Pharmacol Ther 1981;30:687-92.
19. Marshall JR, Graham S, Byers T, et al. Diet and smoking in the epidemiology of cancer of the cervix. JNCI 1983;70:847-51.
20. Trevathan E, Layde P, Webster LA, et al. Cigarette smoking and dysplasia and carcinoma in situ of the uterine cervix. JAMA 1983;250:499-502.
21. Lyon JL, Gardner JW, West DW. Smoking and carcinoma in situ of the uterine cervix. Am J Public Health 1983;73:558-62.
22. Buckley JD, Harris RWC, Doll R, et al. Case-control study of the husbands of women with dysplasia or carcinoma of the cervix uteri. Lancet 1981;2:1010-15.
23. Brown DC, Pereira L, Garner JB. Cancer of the cervix and the smoking husband. Can Fam Physician 1982;28:499-502.
24. Vessey MP, Doll R, Jones K, et al. An epidemiological study of oral contraceptives and breast cancer. Br Med J 1979;1:1757-60.
25. Doll R, Gray R, Haffner B, et al. Mortality in relation to smoking: 22 years' observations on female British doctors. Br Med J 1980;280:967-71.
26. Porter JB, Jick H. Breast cancer and cigarette smoking (letter). N Engl J Med 1983;309:186.
27. Rosenberg L, Schwingl PJ, Kaufman DW, et al. Breast cancer and cigarette smoking. N Engl J Med 1984;310:92-4.
28. Petrakis NL. Nicotine in breast fluid of nonlactating women. Science 1978;199:303-5.
29. Sandler DP, Everson RB, Wilcox AJ, et al. Cancer risk in adulthood from early life exposure to parent's smoking. Am J Public Health, in press.

2023513169

Source: https://www.industrydocuments.ucsf.edu/docs/gfvj0000